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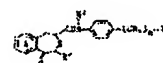
**AU5194999A** ☐ **20000228****Title:** (ENG) Benzothiepin derivatives, process for the preparation of the same and uses thereof**Application Number:** AU 5194999 D**Application (Filing) Date:** 19990806**Priority Data:** JP 22506598 19980807 A X; JP 9904269 19990806 W V;**Inventor(s):** YASUMA TSUNEO ; MAKINO HARUHIKO ; MORI AKIRA**Assignee/Applicant/Grantee:** TAKEDA CHEMICAL INDUSTRIES LTD**Other Abstracts for Family Members:** CHEMABS132(13)166242Z; DERABS C2000-205656

[no drawing available]

**CA2339662A1** ☐ **20000217****Title:** (ENG) BENZOTHIOPIN DERIVATIVES, THEIR PRODUCTION AND USE**Abstract:** Compounds represented by general formula (I) or salts thereof, which exhibit osteogenesis- and chondrogenesis-accelerating effects and are thus useful as drugs; and prodrugs of both: wherein A is an optionally substituted benzene ring; R1 is an optionally substituted nonaromatic heterocyclic group; R2 and R3 are each hydrogen or optionally substituted hydrocarbyl; and n is an integer of 0 to 3.**Application Number:** CA 2339662 A**Application (Filing) Date:** 19990806**Priority Data:** JP 22506598 19980807 A X; JP 9904269 19990806 W V;**Inventor(s):** YASUMA TSUNEO JP ; MAKINO HARUHIKO JP ; MORI AKIRA JP**Assignee/Applicant/Grantee:** TAKEDA CHEMICAL INDUSTRIES LTD JP**Last Modification Date:** 20040303**IPC (International Class):** C07D41712; C07D49504; A61K03155**Publication Language:** ENG**Other Abstracts for Family Members:** CHEMABS132(13)166242Z; DERABS C2000-205656[ERO Register](#)**EP1103552A1** ☐ **20010530** [FullText](#)**Title:** (ENG) BENZOTHIOPIN DERIVATIVES, PROCESS FOR THE PREPARATION OF THE SAME AND USES THEREOF**Abstract:** (ENG)

The invention provides compounds of the formula: wherein the ring A is an optionally substituted benzene ring; R1 is an optionally substituted non-aromatic heterocyclic group; R2 and R3 are independently hydrogen atom or an optionally substituted hydrocarbon group; n is an integer of 0 - 3; or salts thereof, which are useful as medicines having an osteogenesis promoting effect and chondrogenesis promoting effect.

The present invention relates to an amine compound having an excellent effect of inhibiting production and/or secretion of amyloid-b protein, a production and use thereof. Especially, it is effective for preventing and/or treating, for example,



neurodegenerative diseases, amyloid angiopathy, neurological disorders caused by cerebrovascular disorders, and so forth.

**Application Number:** EP 99936994 A

**Application (Filing) Date:** 19990806

**Priority Data:** JP 9904269 19990806 W V; JP 22506598 19980807 A I;

**Inventor(s):** YASUMA TSUNEO JP ; MAKINO HARUHIKO JP ; MORI AKIRA JP

**Assignee/Applicant/Grantee:** TAKEDA CHEMICAL INDUSTRIES LTD JP

**Last Modification Date:** 20040427

**IPC (International Class):** C07D41712; C07D49504; A61K03155

**ECLA (European Class):** C07D49504

**Designated Countries:**

- Designated States: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

**Publication Language:** ENG

**Agent(s):** Caffin, Lee 00062327 Takeda Euro Patent Office, 10 Charles II Street London SW1Y 4AA GB

**Other Abstracts for Family Members:** CHEMABS132(13)166242Z; DERABS C2000-205656

**Non-Patent Citations:**

- DATABASE CA AEOnlineUE CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; PIECHACZEK, JANINA ET AL: "N-Substituted 2-piperidin one derivatives. II" retrieved from STN Database accession no. 70:47245 XP002220972 & ACTAPOL. PHARM. (1968), 25(3), 259-62 ,
- DATABASE CA AEOnlineUE CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; EVANS, B. A. J. ET AL: "Screening and determination of kinetic parameters of aromatase inhibitors using human genital skin fibroblasts" retrieved from STN Database accession no. 120:235239 XP002220973 & JOURNAL OF ENZYME INHIBITION (1993), 7(3), 203-12 ,
- DATABASE CA AEOnlineUE CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; MOLONEY, GERARD P. ET AL: "A Novel Series of 2,5-Substituted Tryptamine Derivatives as Vascular 5HT1B/1D Receptor Antagonists" retrieved from STN Database accession no. 127:81320 XP002220974 & JOURNAL OF MEDICINAL CHEMISTRY (1997), 40(15), 2347-2362 ,
- See also references of WO 0008018A1

**Patents Cited:**

- WO9951590 A E 0
- WO9732863 A X 0
- WO9520588 A X 0
- WO9320073 A X 0
- EP0389699 A X 0
- DD98094 A X 0

**Additional Information:**

- Date of Application deemed Withdrawn 20031008
- Date of request for examination 20010228
- Date of dispatch of first examination report 20030327
- Patent bulletin/ gazette information 20040421 200417
- Date of drawing up and dispatch of supp. search report(A4) 20021129
- PCT application data JP1999004269 19990806 JPN
- PCT publication data WO2000008018 20000217 200007

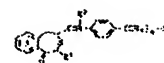
EPO Register

EP1103552A4 ☐ 20030115 FullText

**Title:** (ENG) BENZOTHIOPIN DERIVATIVES, PROCESS FOR THE PREPARATION OF THE SAME AND USES THEREOF

**Abstract:** (ENG)

The invention provides compounds of the formula: wherein the ring A is an optionally substituted benzene ring; R1 is an optionally substituted non-aromatic heterocyclic group; R2 and R3 are independently hydrogen atom or an optionally



substituted hydrocarbon group, n is an integer of 0 - 3; or salts thereof, which are useful as medicines having an osteogenesis promoting effect and chondrogenesis promoting effect.

The present invention relates to an amine compound having an excellent effect of inhibiting production and/or secretion of amyloid- $\beta$  protein, a production and use thereof. Especially, it is effective for preventing and/or treating, for example, neurodegenerative diseases, amyloid angiopathy, neurological disorders caused by cerebrovascular disorders, and so forth.

**Application Number:** EP 99936994 A

**Application (Filing) Date:** 19990806

**Priority Data:** JP 9904269 19990806 W V; JP 22506598 19980807 A I;

**Inventor(s):** YASUMA TSUNEO JP ; MAKINO HARUHIKO JP ; MORI AKIRA JP

**Assignee/Applicant/Grantee:** TAKEDA CHEMICAL INDUSTRIES LTD JP

**Last Modification Date:** 20040427

**IPC (International Class):** C07D41712; C07D49504; A61K03155; C07D27734; C07D23376; C07D21188; C07D26344; C07D26322; C07D27106; C07D27502; C07D21174; C07D27704; C07D29512; A61K03138; C07D49504; C07D337; C07D317

**ECLA (European Class):** C07D49504

**Designated Countries:**

- Designated States: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

**Publication Language:** ENG

**Agent(s):** Caffin, Lee 00062327 Takeda Euro Patent Office, 10 Charles II Street London SW1Y 4AA GB

**Other Abstracts for Family Members:** CHEMABS132(13)166242Z; DERABS C2000-205656

**Non-Patent Citations:**

- DATABASE CA AEOnlineUE CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; PIECHACZEK, JANINA ET AL: "N-Substituted 2-piperidin one derivatives. II" retrieved from STN Database accession no. 70:47245 XP002220972 & ACTAPOL. PHARM. (1968), 25(3), 259-62 ,
- DATABASE CA AEOnlineUE CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; EVANS, B. A. J. ET AL: "Screening and determination of kinetic parameters of aromatase inhibitors using human genital skin fibroblasts" retrieved from STN Database accession no. 120:235239 XP002220973 & JOURNAL OF ENZYME INHIBITION (1993), 7(3), 203-12 ,
- DATABASE CA AEOnlineUE CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; MOLONEY, GERARD P. ET AL: "A Novel Series of 2,5-Substituted Tryptamine Derivatives as Vascular 5HT<sub>1B/1D</sub> Receptor Antagonists" retrieved from STN Database accession no. 127:81320 XP002220974 & JOURNAL OF MEDICINAL CHEMISTRY (1997), 40(15), 2347-2362 ,
- See also references of WO 0008018A1

**Patents Cited:**

- WO9951590 A E 0
- WO9732863 A X 0
- WO9520588 A X 0
- WO9320073 A X 0
- EP0389699 A X 0
- DD98094 A X 0

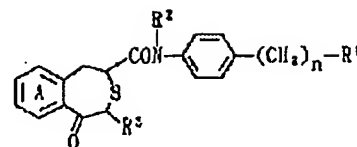
**Additional Information:**

- Date of Application deemed Withdrawn 20031008
- Date of request for examination 20010228
- Date of dispatch of first examination report 20030327
- Patent bulletin/ gazette information 20040421 200417
- Date of drawing up and dispatch of supp. search report(A4) 20021129
- PCT application data JP1999004269 19990806 JPN
- PCT publication data WO2000008018 20000217 200007

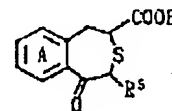
JP2000109480A ☐ 20000418 FullText**Title:** (ENG) BENZOTHIPIEPINE DERIVATIVE, AND ITS PRODUCTION AND USE**Abstract:** (ENG)

**PROBLEM TO BE SOLVED:** To obtain a new compound having strong bone formation promotion, chondrogenesis promotion, cartilage breakdown prevention functions or the like, excellent in stability, oral absorbability, intracorporeal availability or the like, and useful for prevention or treatment of bone and cartilage diseases, e.g. osteoporosis, bone fracture and cartilage deficiency.

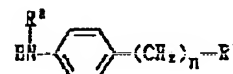
**SOLUTION:** This compound is shown by formula I [ring A is (substituted) benzene; R1 is a (substituted) nonaromatic heterocyclic ring; R2 and R3 are each H or a (substituted) hydrocarbon; and (n) is 0 to 3], preferably N-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenyl]-1,2,4,5-tetrahydro-7,8-methylenedioxy-4-methyl-5-oxo-3-benzothiepine-2-carboxide, or the like. The compound shown by formula I is obtained by reacting a compound shown by formula II, its reactive derivative at its carboxy group or salt thereof, with a compound shown by formula III, its reactive derivative at its amino group or salt thereof, preferably at about -5 to 50°C.



I



II



III

**Application Number:** JP 22358099 A**Application (Filing) Date:** 19990806**Priority Data:** JP 22358099 19990806 A X; JP 22506598 19980807 A X;**Inventor(s):** YASUMA TSUNEO ; MAKINO HARUHIKO ; MORI AKIRA**Assignee/Applicant/Grantee:** TAKEDA CHEMICAL INDUSTRIES LTD

**IPC (International Class):** C07D41712; A61K03140; A61K03141; A61K031415; A61K03142; A61K031427; A61K031445; A61K031535; A61K03154; A61P01900; C07D20740; C07D21174; C07D21188; C07D23372; C07D26344; C07D27106; C07D27704; C07D49504

**Other Abstracts for Family Members:** CHEMABS132(13)166242Z; DERABS C2000-205656

US2002128308A1 ☐ 20020912 FullText**Title:** (ENG) Benzothiepine derivatives, their production and use**Abstract:** (ENG)

The invention provides compounds of the formula:

**Application Number:** US 4478702 A**Application (Filing) Date:** 20020111**Priority Data:** US 4478702 20020111 A A; JP 22506598 19980807 A A; US 74485701 20010130 A A;**Related Application(s):** 09/744857 20010130 6355672 US GRANTED**Inventor(s):** YASUMA TSUNEO JP ; MAKINO HARUHIKO JP ; MORI AKIRA JP**Assignee/Applicant/Grantee:** YASUMA TSUNEO JP; MAKINO HARUHIKO JP; MORI AKIRA JP**Last Modification Date:** 20040514**IPC (International Class):** C07D33708; A61K03138

**ECLA (European Class):** C07D21188; C07D23374; C07D26344D; C07D26344F; C07D27704; C07D29512A3; C07D49504

**US Class:** 514431; 549012

**Other Abstracts for Family Members:** CHEMABS132(13)166242Z; DERABS C2000-205656

US6355672B1 ☐ 20020312 FullText**Title:** (ENG) Benzothiepin derivatives, process for the preparation of the same and uses thereof**Abstract:** (ENG)

The invention provides compounds of the formula:

wherein the ring A is an optionally substituted benzene ring; R 1 is an optionally substituted non-aromatic heterocyclic group; R 2 and R 3 are independently hydrogen atom or an optionally substituted hydrocarbon group; n is an integer of 0-3; or salts thereof, which are useful as medicines having an osteogenesis promoting effect and chondrogenesis promoting effect.

The present invention relates to an amine compound having an excellent effect of inhibiting production and/or secretion of amyloid- $\beta$  protein, a production and use thereof. Especially, it is effective for preventing and/or treating, for example, neurodegenerative diseases, amyloid angiopathy, neurological disorders caused by cerebrovascular disorders, and so forth.

**Application Number:** US 74485701 A

**Application (Filing) Date:** 20010130

**Priority Data:** JP 22506598 19980807 A A; JP 9904269 19990806 W V;

**Inventor(s):** YASUMA TSUNEO JP ; MAKINO HARUHIKO JP ; MORI AKIRA JP

**Assignee/Applicant/Grantee:** TAKEDA CHEMICAL INDUSTRIES LTD JP

**Last Modification Date:** 20040823

**IPC (International Class):** C07D33708; A61K03138; A61P01908

**ECLA (European Class):** C07D21188; C07D23374; C07D26344D; C07D26344F; C07D27704; C07D29512A3; C07D49504

**US Class:** 514431; 514096; 5142282; 5142288; 5142328; 5142335; 514336; 514372; 514376; 514378; 514380; 514397; 544060; 544061; 544062; 544175; 544197; 544202; 548188; 548196; 548213; 548227; 548229; 548243; 5483114; 5483117; 548526; 548527; 549009

**Agent(s):** Chao Mark ; Ramesh Elaine M.

**Examiner Primary:** Solola, T. A.

**Examiner Assistant:** D'Souza, Andrea

**Other Abstracts for Family Members:** CHEMABS132(13)166242Z; DERABS C2000-205656

**Non-Patent Citations:**

- Ahluwalia, et al., 1986, Indian J. Chem., 25B(5), 502-4.\*
- Akiyama, et al. "TAK-778, a Novel Synthetic 3-Benzothiepin Derivative, promotes Chondrogenesis In Vitro and in Vivo" Biochemical and Biophysical Research Communications 261:131-138 (1999).

**Patents Cited:**

- US5071841 19911200 A Sohda et al. 514096 OTHER
- US5158943 19921000 A Sohda et al. 514096 OTHER
- US5952512 19990900 A Maeda et al. 549012 OTHER
- US6190695 20010200 B1 Hoshino et al. 424464 OTHER
- EP376197 19900700 OTHER
- EP460488 19911200 OTHER
- EP719782 19960700 OTHER
- JP8231569 19960800 EXAMINER
- WO8601407 19860300 EXAMINER
- WO9413642 19940600 EXAMINER
- WO9639134 19961200 OTHER
- WO9965474 19991200 OTHER

**Assignments Reported to USPTO:**

**Reel/Frame:** 11749/0507      **Date Signed:** 20001228      **Date Recorded:** 20010427  
**Assignee:** TAKEDA CHEMICAL INDUSTRIES, LTD. 1-1, DOSHOMACHI 4-CHOME, CHUO-KU OSAKA 541-0 JAPAN  
**Assignor:** MAKINO, HARUHIKO; MORI, AKIRA; YASUMA, TSUNEO  
**Corres. Addr.:** TAKEDA PHARMACEUTICALS NO. AMERICA, INC. PHILIPPE Y. RIESEN INTELLECTUAL PROPERTY DEPARTMENT 475 HALF DAY ROAD, SUITE 500 LINCOLNSHIRE, IL 60069  
**Brief:** ASSIGNMENT OF ASSIGNORS INTEREST (SEE DOCUMENT FOR DETAILS).

**Additional Information:**

- Number of claims 13
- Exemplary claim number(s) 1
- National classifications searched , 548188 , 548196 , 548213 , 548227 , 548229 , 548243 , 5483117 , 5483114 , 548526 , 548527 , 549009 , 544060 , 544061 , 544062 , 544197 , 544202 , 544175 , 514431 , 514336 , 514372 , 514376 , 514378 , 514380 , 514397 , 5142282 , 5142288 , 5142328 , 5142335 , 514096
- Number of drawing sheets 0
- Number of figures 0
- PCT application data JP9904269 19990806 WO
- PCT publication data WO0008018 20000217 WO A

**US6531604B2** ☐ **20030311** [FullText](#)

**Title:** (ENG) Benzothiepine derivatives, their production and use

**Abstract:** (ENG)

The invention provides compounds of the formula:

wherein the ring A is an optionally substituted benzene ring; R 1 is an optionally substituted non-aromatic heterocyclic group; R 2 and R 3 are independently hydrogen atom or an optionally substituted hydrocarbon group; n is an integer of 0-3; or salts thereof, which are useful as medicines having an osteogenesis promoting effect and chondrogenesis promoting effect.

The present invention relates to an amine compound having an excellent effect of inhibiting production and/or secretion of amyloid-b protein, a production and use thereof. Especially, it is effective for preventing and/or treating, for example, neurodegenerative diseases, amyloid angiopathy, neurological disorders caused by cerebrovascular disorders, and so forth.

**Application Number:** US 4478702 A

**Application (Filing) Date:** 20020111

**Priority Data:** US 4478702 20020111 A A; JP 22506598 19980807 A A; US 74485701 20010130 A A;

**Inventor(s):** YASUMA TSUNEO JP ; MAKINO HARUHIKO JP ; MORI AKIRA JP

**Assignee/Applicant/Grantee:** TAKEDA CHEMICAL INDUSTRIES LTD JP

**Last Modification Date:** 20040514

**IPC (International Class):** C07D21140; C07D27502; C07D26302; C07D23302

**ECLA (European Class):** C07D21188; C07D23374; C07D26344D; C07D26344F; C07D27704; C07D29512A3; C07D49504

**US Class:** 546219; 548213; 548227; 5483201

**Agent(s):** Chao Mark ; Ramesh Elaine M.

**Examiner Primary:** Chang, Cella

**Examiner Assistant:** Small, Andrea D.

**Other Abstracts for Family Members:** CHEMABS132(13)166242Z; DERABS C2000-205656

**Non-Patent Citations:**

- Plechaczek, et al, 1968, Acta Pol. Pharm. 25(3), 259-262.\*
- Artico, et al, 1998, Bioorg. Med. Chem, 8(12), 1493-1498.\*
- Siemion, et al, 1990, Int. J. Pept. Protein Res., 36(6), 506-514.\*
- Wang, et al, 1990, Gaodeng Xuexiao Huaxue Xuebao, 11(8), 894-6.\*
- Akiyama, et al. "TAK-778, a Novel Synthetic 3-Benzothiepin Derivative, Promotes Chondrogenesis in Vitro and in Vivo" Biochemical and Biophysical Research Communications 261: 131-138(1999).
- Ahluwalia, et al. "Some new thiazole derivatives from dihydrochalcones" Indian J. Chem., 25B(5), 502-4(1986)-- Abstract.

**Patents Cited:**

- US4722892 19880200 A Meares et al. OTHER
- US5071841 19911200 A Sohda et al. OTHER
- US5158943 19921000 A Sohda et al. OTHER
- US5683997 19971100 A Buehlmaier et al. OTHER
- US5952512 19990900 A Maeda et al. OTHER
- US6043254 20000300 A Grell et al. 514310 EXAMINER
- US6190695 20010200 B1 Hoshino et al. OTHER
- EP376197 19900700 OTHER
- EP460488 19911200 OTHER
- EP719782 19960700 OTHER
- WO9320073 19931000 EXAMINER
- WO9639134 19961200 OTHER
- WO9712870 19970400 EXAMINER
- WO9732863 19970900 EXAMINER
- WO9858934 19981200 EXAMINER
- WO9965474 19991200 OTHER

**Additional Information:**

- Number of claims 2
- Exemplary claim number(s) 1
- National classifications searched , 548566 , 548546 , 548189 , 548146 , 548227 , 548228 , 548229 , 548213 , 548214 , 5483195 , 5483201 , 546219 , 546216 , 546229 , 544166 , 544059
- Number of drawing sheets 0
- Number of figures 0

EPO Register

WO2000008018A1 20000217 FullText

**Title:** (ENG) BENZOTHIEPIN DERIVATIVES, PROCESS FOR THE PREPARATION OF THE SAME AND USES THEREOF

**Abstract:** (ENG)

Compounds represented by general formula (I) or salts thereof, which exhibit osteogenesis- and chondrogenesis-accelerating effects and are thus useful as drugs; and prodrugs of both: wherein A is an optionally substituted benzene ring; R 1 is an optionally substituted nonaromatic heterocyclic group; R 2 and R 3 are each hydrogen or optionally substituted hydrocarbyl; and n is an integer of 0 to 3.

**Application Number:** JP 9904269 W

**Application (Filing) Date:** 19990806

**Priority Data:** JP 22506598 19980807 A I;

**Inventor(s):** YASUMA TSUNEO JP ; MAKINO HARUHIKO JP ; MORI AKIRA JP

**Assignee/Applicant/Grantee:** TAKEDA CHEMICAL INDUSTRIES LTD JP;  
YASUMA TSUNEO JP; MAKINO HARUHIKO JP; MORI AKIRA JP

**Last Modification Date:** 20050526

**IPC (International Class):** C07D41712; C07D49504; A61K03155

**ECLA (European Class):** C07D49504; C07D21188; C07D23374; C07D26344D;  
C07D26344F; C07D27704; C07D29512A3

**Designated Countries:**

- Designated States: AE AL AM AU AZ BA BB BG BR BY CA CN CR CU CZ EE GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK SL TJ TM TR TT UA US UZ VN YU ZA
- Regional Treaties: GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

**Publication Language:** JAP

**Agent(s):** ASAHINA, Tadao Osaka Plant of Takeda Chemical Industries, Ltd., 17-85, Jusohonmachi 2-chome, Yodogawa-ku, Osaka-shi, Osaka 532-0024 JP

**Other Abstracts for Family Members:** CHEMABS132(13)166242Z; DERABS C2000-205656

**Other Abstracts for This Document:** CHEMABS132(13)166242Z; DERABS C2000-205656

**Non-Patent Citations:**

- See also references of EP 1103552A1

**Patents Cited:**

- JP8231569 A X 0
- JP3232880 A Y 0
- JP4364179 A A 0



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